Bikuspidna aortna valvula – prikaz slučaja

Bicuspid Aortic Valve – A Case Report

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SAŽETAK: Bikuspidna aortna valvula najčešća je prirođena srčana bolest, ali se u užemu smislu ne smatra bolešću, nego predispozicijom za njezin razvoj. Dijapazon prezentacije i vrijeme pojave bolesti takvog aortnog zalistka vrlo je raznovrstan. U našoj praksi bolesnike koji se prezentiraju u ranoj dobi te osobito ako imaju pridružene anomalije (aneurizmu aorte, koarktaciju, membranu), razmatramo u okviru grupe za kongenitalne srčane bolesti, osobito stoga što, kako je ovdje prikazano, takvi bolesnici trebaju trajno praćenje i često višekratne intervencije. Prikazani je bolesnik i dobar primjer kombinacije prirođenog defekta i „stečene" (koronarne) bolesti srca, što je jedna od karakteristika populacije s prirođenim srčanim bolestima, u dugotrajnom praćenju.

SUMMARY: Bicuspid aortic valve is the most common congenital heart disease, although in the narrow sense it is not considered a disease but a predisposition for its development. The range of manifestations and the time of the onset of such a disease of the aortic valve vary greatly. In our practice, patients with manifestation at an early age, and especially those with accompanying anomalies (aortic aneurysm, coarctation, membrane), are classified under of congenital heart diseases due to the fact that, as is shown herein, such patients require constant monitoring and often multiple interventions. The patient described here is a good example of a combination of congenital disorder and coronary heart disease, which is characteristic for patients with congenital heart diseases under long-term monitoring.

KLJUČNE RIJEČI: bikuspidni aortni zalistak, aortna stenoza, subaortna membrana, koronarna aneurizma, zamjena aortnog zalistka.

KEYWORDS: bicuspid aortic valve, aortic stenosis, subaortic membrane, coronary aneurysm, aortic valve replacement.

CITATION: Cardiol Croat. 2016;11(1-2):50–54. | **DOI:** http://dx.doi.org/10.15836/ccar2016.50

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Uvod

Bikuspidna aortna valvula (BAV) najčešća je prirođena srčana bolest odraslih, s kojom se svakodnevno susrećemo u kliničkoj praksi. Iako je u studijama dokazano da ne utječe na preživljenje, važna je jer su tijekom života ovakvi bolesnici suočeni s mnogobrojnim komplikacijama te posljedičnim učestalim intervencijama koje utječu na kvalitetu života i kardiovaskularne ishode. Kako je riječ o bolesti zalistka, ali i aortne stijenke, kojoj je dijelom poznata i genetska podloga, suočeni smo sa spektrom manifestacija bolesti – od potpuno asimptomatske u zreloj dobi do simptomatske bolesti s ranom potrebom za intervencijom već u djetinjstvu.

Introduction

Bicuspid aortic valve (BAV) is the most common congenital heart disease in adults, one we encounter daily in clinical practice. Although studies show that it does not affect survival, it is an important issue because affected patients are faced with numerous complications and, as a consequence of that, frequent interventions that impact quality of life and cardiovascular outcomes. Since this is a disease of the valve but also of the aortic wall, the genetic basis of which is partially known, we are faced with an entire range of disease manifestations – from an entirely asymptomatic disease in adulthood to symptomatic disease with needing intervention in childhood.

RECEIVED:
January 14, 2016

ACCEPTED:
January 31, 2016

Bolest zahvaća 0,5 – 2 % ukupne populacije, triputa je češća u muškaraca i javlja se familijarno (10 % u prvom koljenu). U podlozi je poremećaj valvulogeneze sa stvaranjem dvaju obično nejednakih listića; zbog poremećaja u sintezi fibrilina-1 lošija je kvaliteta zalistka i stijenke aorte, a zbog promjena na zalistku dolazi i do posljedičnih hemodinamskih turbulencija koje uzrokuju dodatna oštećenja.

Tipični oblik BAV-a (tip 1) nastaje srastanjem desnog i lijevog koronarnog listića s posljedičnom anterioposteriornom orijentacijom. Tip 2 je tzv. atipični, s lijevo-desnom orijentacijom (srašteni su desni i nekoronarni listić), a najrjeđi oblik nastaje fuzijom lijevog i nekoronarnog listića. Na mjestu sraštenja komisura, najčešće se vidi zadebljanje, tzv. raphe. Uz tip 1 češće dolazi do stenoze zalistka u odrasloj dobi, uz dilataciju uzlazne aorte i koarktaciju aorte, dok kod tipa 2 dolazi do ranijih komplikacija sa zahvaćanjem listića već u dječjoj dobi te dilatacijom i ascendentne i luka aorte.

Najčešće pridružene anomalije jesu aortopatija (češća u tipu 2) i koarktacija aorte (u 20% svih bolesnika s BAV-om), a rjeđe VSD, Ebsteinova anomalija, sindrom hipoplastičnoga lijevog srca, abnormalna anatomija koronarnih arterija, patent duktus arteriozus, ASD i bikuspidna pulmonalna valvula.

Prezentacija i klinički tijek ovise o razvijenim komplikacijama. Najčešća je aortna stenoza, koja nastaje degeneracijom i kalcifikacijom valvule te obično zahtijeva intervenciju u srednjoj životnoj dobi. Aortna regurgitacija posljedica je najčešće prolapsa zalistka, endokarditisa, dilatacije korijena aorte ili miksoidne degeneracije valvule te obično zahtijeva intervenciju u mlađoj odrasloj dobi (10 – 40 godina). Endokarditis nije čest (pojavljuje se u manje od 2% bolesnika s BAV-om), ali ima lošiji ishod u odnosu prema zdravoj populaciji. Što se tiče komplikacija vezanih za aortu (aneurizma, disekcija i ruptura aorte), aneurizma uzlazne aorte vrlo je česta (čak do 80 %), dok su ostale dvije komplikacije rjeđe, ali s visokom stopom smrtnosti (incidencija disekcije 1 – 4 % bolesnika s BAV-om, ali devet puta češća nego u općoj populaciji).[1,2]

Dijagnoza se postavlja prije svega ehokardiografski. Obično je dovoljan već transtorakalni ehokardiografski pregled za utvrđivanje bolesti i postojećih komplikacija, kao i za redovito praćenje. Osobita se pozornost posvećuje procjeni valvularne greške, mjerenju dimenzija uzlazne aorte, progresiji valvularne greške i dilatacije aorte te otkrivanju pridruženih anomalija, npr. koarktacije aorte. U kompliciranijim slučajevima ili kada se ne može (obično zbog obilja kalcifikata) procijeniti broj listića te pri preoperativnoj obradi, bit će potreban i transezofagijski ultrazvuk srca, a za praćenje aortopatije CT ili MR aortografija.[3] Učestalost kontrolnih slikovnih pregleda obično je individualna, ali svakako treba biti kontinuirana.

Specifičnog liječenja, naravno, nema, ali treba liječiti stanja koja mogu uzrokovati komplikacije, kao što je npr. liječenje arterijske hipertenzije, sprečavanje aortopatije (beta-blokatorima ili sartanima), profilaksa endokarditisa itd. Naposljetku, ipak će većina bolesnika zahtijevati neki oblik intervencije tijekom života. Ponajprije bit će riječ o zamjeni ili, rjeđe, balonskoj dilataciji zalistka te će se u dogovoru s bolesnikom odabrati optimalan zahvat i tip zalistka. Naravno, nakon intervencije ovi bolesnici i dalje zahtijevaju naš strogi nadzor, a

The disease affects 0.5-2.0% of the total population, is three times as common among men, and occurs familially (10% among first cousins). It is based on a valvulogenesis disorder that leads to the creation of two usually unequal leaflets; due to a disorder in fibrillin-1 synthesis the valve and the aortic wall are of poorer quality, and the changes in the valve also lead to further hemodynamic turbulence that causes additional damage.

The typical BAV (type 1) occurs as a result of a fusion of the right and left coronary leaflet, with consequential anteroposterior orientation. Type 2, also known as atypical, has a right-left orientation (there is a fusion between the right and the non-coronary leaflet), and the rarest type is the result of a fusion of the left and the non-coronary leaflet. At the place where the commissures have fused there is commonly a thicker area, also known as "raphe". Type 1 is more commonly associated with valve stenosis in adulthood, as well as the dilatation of the ascending aorta and the coarctation of the aorta, whereas type 2 is associated with earlier complications in childhood and the dilatation of both the ascending aorta and the aortic arch.

The most common associated anomalies are aortopathy (more common in type 2) and the coarctation of the aorta (in 20% of all patients with BAV), whereas less common anomalies include ventricular septal defect (VSD), Ebstein's anomaly, hypoplastic left heart syndrome, abnormal anatomy of coronary arteries, patent ductus arteriosus, atrial septal defect (ASD), and bicuspid pulmonic valve.

The presentation and the clinical progression depend on the complications that have developed. Most common is aortic stenosis, a result of degeneration and calcification of the valve and usually requiring intervention in middle age. Aortic regurgitation is most commonly the result of valve prolapse, endocarditis, dilatation of the aortic root, or myxoid degeneration of the valve, and usually requires intervention in early adult age (10-40 years). Endocarditis is not common (it occurs in less than 2% of patients with BAV) but outcomes are worse in comparison with the healthy population. Regarding the complications in the aorta (aortic aneurysm, dissection, and rupture), aneurysm of the ascending aorta is very common (even up to 80%) whereas the other two complications are less frequent, but have a high rate of mortality (the incidence of dissection is 1-4% in patients with BAV, but is nine times more common than in the general population).[1,2]

Echocardiography is the primary diagnostic method. Usually only a transthoracic echocardiographic examination is sufficient for the identification of the disease and any existing complications, as well as for further monitoring. Special attention is paid to the assessment of the valve disease, the measurement of the dimensions of the ascending aorta, the progression of the valve disease, the dilatation of the aorta, and the discovery of associated anomalies, e.g. aortic coarctation. In more complicated cases or when it is impossible to assess (usually due to the amount of calcification) the number of leaflets and during preoperative preparation, it is necessary do perform transesophageal heart ultrasound, whereas monitoring aortopathy requires a computed tomography (CT) or magnetic resonance (MR) aortography.[3] The frequency of

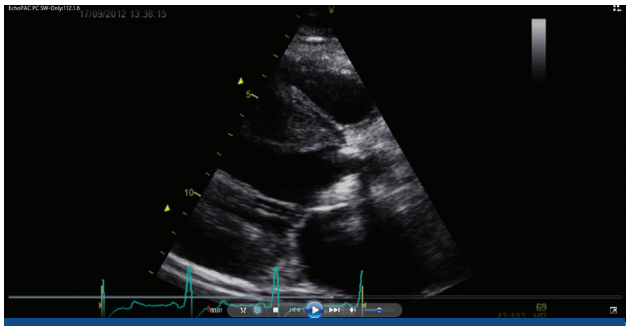

FIGURE 1. Extreme hypertrophy of the left ventricle in patient with severe aortic stenosis.

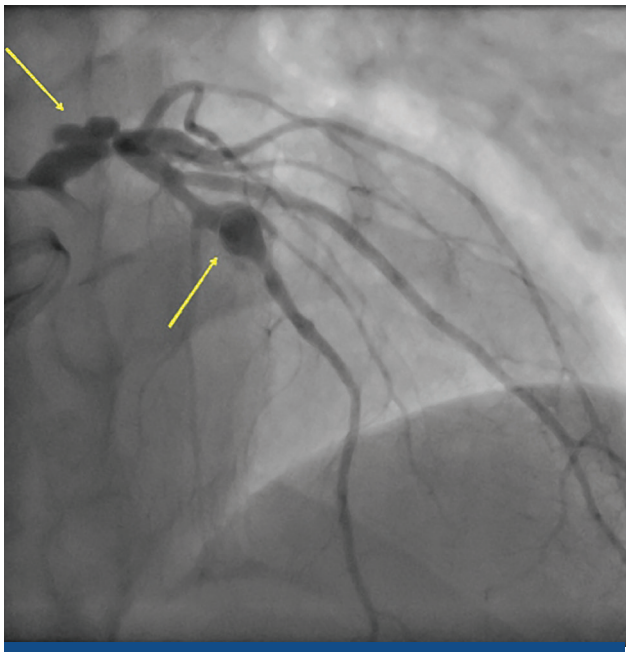

FIGURE 3. Angiogram of the left coronary artery. Note coronary artery aneurysms.

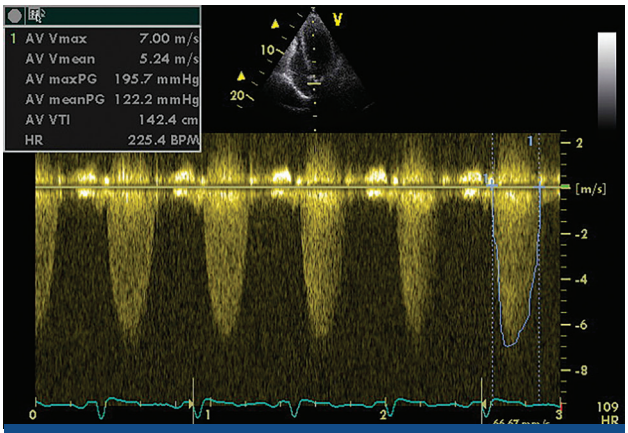

FIGURE 2. Continuous-wave Doppler signal of severe aortic stenosis jet shows high velocities.

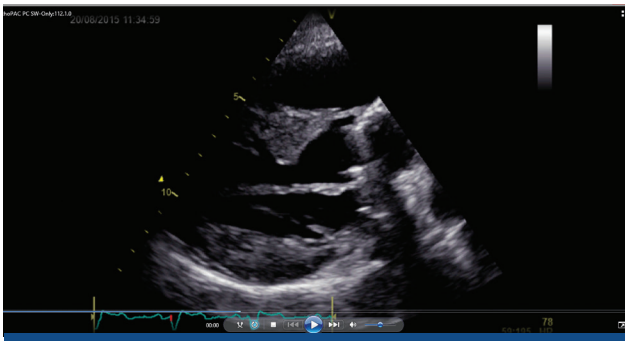

FIGURE 4. Echocardiography after coronary artery bypass grafting with dilatation of the aortic anulus, resection of the left ventricular outflow tract and implantation of the SJM Regent 21 valve.

važnost ove postavke naglašavamo i prikazom jednog slučaja iz kliničke prakse.

Prikaz slučaja

Četrdesetjednogodišnji muškarac u kojeg se od djetinjstva zna za šum na srcu, upućen je 2010. godine na ehokardiografski pregled zbog pojava stenokardija u naporu. Na učinjenom transtorakalnom ehokardiografskom pregledu (TTE) prikazana je je (**slika 1**, **slika 2**) obilno kalcificirana bikuspidna aortna valvula s teškom aortnom stenozom i očuvanom sistoličkom funkcijom lijeve klijetke (maks. gradijent 195 mmHg, srednji 122 mmHg, AVA 0,6 cm^2, AVA/BSA 0,3 cm^2/m^2, EF LV 60 %). Obavljenom koronarografijom isključena je bolest epikardijalnih arterija te je bolesnik referiran kardijalnom kirurgu. Čekajući na preporučeni kardiokirurški zahvat, u svibnju 2012. god. ponovno se javlja nakon dvije godine u ambulantu zbog simptoma kardijalne dekompenzacije. Ponovljen je TTE

follow-up imaging examinations is usually determined individually for each patient, but should certainly be regular.

There is of course no specific treatment, but conditions that can lead to complications should be treated, for example in cases of arterial hypertension, prevention of aortopathy (using beta blockers or ARBs), endocarditis prophylaxis, etc. After all, most patients will require some form of intervention in their lifetime. This will primarily mean the replacement of the valve or, in rarer cases, balloon dilatation of the valve, and the physician will consult the patient when deciding on the optimal intervention and type of valve. Of course, after the intervention these patients still require our strict supervision; the importance of this will be emphasized using the example of one case from clinical practice.

Case report

A 41-year-old man who had had a confirmed heart murmur since childhood was given an echocardiographic examination due to the angina in exertion in 2010. A transthoracic echocardiography (TTE) examination (**Figure 1**, **Figure 2**) showed ample calcification in the bicuspid aortic valve with severe aortic stenosis and preserved left ventricular systolic

kojim je prikazana znatna redukcija sistoličke funkcije lijeve klijetke (EF 30 %, AVA 0,5 cm^2, maks. PG 137 mmHg, srednji 80 mmHg, nema dilatacije ascendentne aorte), a koronarografijom se sada prikazala aneurizma na prijelazu proksimalne u srednju LAD veličine 11 x 8 mm (**slika 3**). Indiciran je hitni zahvat zamjene aortne valvule, a odlučeno je da će se aneurizma LAD-a riješiti u drugom aktu postavljanjem stent grafta u slučaju dokaza ishemije miokarda. Tako je bolesniku 11. rujna 2012. god. izvedena zamjena aortne valvule mehaničkom (ATS Medical 21 mm). Intraoperativno se prikazala i subaortna membrana (ispod lijevog i desnog koronarnog kuspisa) koja je u istom aktu resecirana te je učinjena i dekalcifikacija izgonskoga trakta lijeve klijetke i anulusa aortne valvule. Postoperativno se već nakon nekoliko dana pratio oporavak sistoličke funkcije lijeve klijetke (LVEF 55 %), ali uz i dalje visoke gradijente preko aortne valvule (maksimalni gradijent 83 mmHg) i blagu aortnu regurgitaciju.

Međutim, nakon operacije bolesnik i dalje ima tegobe u smislu intolerancije napora uz bolove u prsima. U listopadu 2014. god. učinjen je SPECT miokarda kojim je dokazana ishemija apeksa i lateralne stijenke lijeve klijetke. Na sljedećemu kontrolnom ehokardiografskom pregledu bolesnik navodi daljnje pogoršanje tegoba, prema laboratorijskim nalazima, već je duže vrijeme neadekvatno antikoaguliran, uz hemodinamski nepovoljne parametre protoka preko mehaničke AV (maksimalni gradijent 100 mmHg, umjerena AR, intrakavitarni gradijent 20 mmHg, EF 60 %) te je hospitaliziran radi dodatne obrade. Kako su gradijenti preko zalistka bez veće promjene u usporedbi s ranima postoperativnima, a dijaskopijom je isključena i tromboza valvule, utvrđeno je da je riječ o nerazmjeru između veličine umjetne valvule i površine tijela bolesnika (EOA/BSA = 0,70). Ponovljenom koronarografijom pokazale su se dvije tandem sakularne aneurizme do 6 mm u deblu, a distalno deblo i ostijum LAD stenozirani su do 70 %, uz još jednu sakularnu aneurizmu srednje LAD promjera do 8 mm. Indicirana je reoperacija te je poduzeto dvostruko aortokoronarno premoštenje (LAD-LIMA, RIM-VSM), uz proširivanje korijena aorte i resekciju izlaznog dijela lijeve klijetke. Implantirana je SJM Regent 21mm valvula (**slika 4**) s boljom hemodinamikom za ovog bolesnika (očekivani gradijent = 15,6 ± 9,4; srednji = 8,0 ± 4,8; EOA = 2,0 ± 0,7; EOA/BSA = 1,01), a zahvat je protekao bez komplikacija.

U daljnjim kontrolama bolesnik je subjektivno bez tegoba, nema bolova u prsima i dobro podnosi fizičke napore. Kontrolnim ehokardiografskim pregledom utvrđen je široki LVOT nakon miektomije, znatno koncetrično hipertrofičan LV, EF 60 %, maks. gradijent od 49 mmHg, srednji 26 mmHg, AVA 1,6 cm^2, što je zadovoljavajuće.

Rasprava

Vodeći se bolesnikovim tegobama, hemodinamskim performansama valvule te postojanjem dodatne patologije koronarnih arterija koja je, zasigurno, bila barem dijelom uzrok simptoma, bilo je jasno da je ponovna intervencija nužna. No odluku nije bilo lako donijeti. U tome je svakako pomogao tzv. heart team u kojemu su bili bolesnikov nadležni kardiolog, ehosonografičar, te intervencijski kardiolog i kardijalni kirurg. Rizik od reoperacije bio je uvećan, planirani zahvat vrlo opsežan, a ishod upitan jer je bilo jasno da se i nakon miekfunction (max gradient 195 mmHg, mean 122 mmHg, AVA 0.6cm^2, AVA/BSA 0.3cm^2/m^2, EF LV 60%). Coronary angiography excluded the disease of epicardial arteries, and the patient was referred to a cardiac surgeon. After two years, in May of 2012, while waiting for the recommended cardiac surgery, the patient again sought treatment due to symptoms of heart failure. TTE showed a significant reduction in left ventricular systolic function (EF 30%, AVA 0.5cm^2, max PG 137 mmHg, mean 80 mmHg, no dilatation of the ascending aorta), and coronary angiography now showed an aneurysm on the transition from the proximal into mid LAD that was 11×8 mm (**Figure 3**) in size. An emergency surgical procedure was indicated in order to replace the aortic valve, and it was decided to resolve the LAD aneurysm afterwards by putting in a stent graft in case myocardial ischemia was established. On September 11, 2012 patient underwent aortic valve replacement with ATS Medical 21 mm valve. During operation a subaortic membrane was discovered (under the left and right coronary cusp) and resected in the same operation, and decalcification of the left ventricular outflow tract and the annulus of the aortic valve was also performed. Already several days after the procedure there was improvement of the left ventricular systolic function (LVEF 55%), but with high gradients over the aortic valve (max gradient 83 mmHg) and mild aortic regurgitation.

However, after the operation the patient still experienced exertion intolerance accompanied by chest pain. In October 2014, a myocardial perfusion SPECT (Single Photon Emission Computed Tomography) was performed and showed ischemia at the apex and lateral wall of the left ventricle. At the next echocardiographic examination the patient claimed his difficulties were becoming more severe. Laboratory tests showed that he had been inadequately anticoagulated for a long period of time, with hemodynamically unfavorable parameters of flow over the mechanical AV (max gradient 100 mmHg, moderate AR, intracavitary gradient 20 mmHg, EF 60%), so he was hospitalized for further testing. Since the gradients over the valve showed no significant change in comparison with early postoperative values, and since diascopy excluded valve thrombosis, a patient prosthesis mismatch (EOA/BSA=0.70) was found to be the cause of the patient's issues. Repeated coronarography showed two tandem saccular aneurysms of up to 6 mm in the trunk, the distal trunk and ostial LAD with up to 70% stenosis, and another saccular aneurysm of mid LAD diameter of up to 8mm. A reoperation was indicated, and a double bypass grafting (LAD-LIMA, RIM-VSM) was performed along with the LV outflow tract resection and aortic root dilatation. An SJM Regent 21 mm valve (**Figure 4**) with a better hemodynamic parameters for this patient was implanted (expected gradient = 15.6±9.4, mid = 8.0±4.8, EOA = 2.0±0.7, EOA/BSA = 1.01), and the operation was performed with no complications. In later follow-up the patient reported no subjective difficulties, no chest pain, and reacting well to physical exertion. An echocardiographic examination found a wide LVOT after myectomy, concentrically hypertrophied LV, EF 60%, max gradient of 49 mmHg, mean 26 mmHg, and AVA 1.6cm^2, which are satisfactory values.

tomije neće moći implantirati mnogo veći zalistak, a izrazita hipertrofija miokarda koja dovodi i do dijastoličke disfunkcije može i dalje uzrokovati tegobe i limitirati bolesnika u svakodnevnim aktivnostima. Naravno, tu je i „životni vijek" umjetnog zalistka te je izgledna i treća reoperacija kasnije tijekom života. Ipak, ako circulus viciozus ne bude prekinut, tlačno opterećenje lijeve klijetke i ishemija vodit će dalje u progresivnu hipertrofiju i fibrozu te poslije u intraktabilno popuštanje srca. Iako je klinički tijek nakon drugog zahvata za sada povoljan, dugoročno nas očekuje praćenje funkcije valvule, praćenje dimenzija ascendentne aorte koja u ovom trenutku nije bila dilatirana, stroga kontrola arterijskoga tlaka, profilaksa endokarditisa te rješavanje svih drugih komorbiditeta koje očekujemo starenjem.

Zaključak

Veliko kliničko iskustvo s obzirom na učestalost bolesti i uglavnom povoljan klinički ishod, ne smiju nas zavarati da iz praćenja „izgubimo" bolesnike u kojih je progresija bolesti spora ili je već učinjena neka vrsta intervencije, jer je i dalje radi o mladoj i ranjivoj populaciji kod koje se očekuje normalan životni vijek, a usto se, naravno, podrazumijeva i dobra kvaliteta života. Stoga je važno imati na umu koje nas sve komplikacije same bolesti te komplikacije provedenih intervencija mogu očekivati, uz kontinuirani nadzor. Prije svega se to odnosi na ehokardiografsko praćenje progresije aortne stenoze i regurgitacije, praćenje dimenzije aorte te procjena veličine i funkcije lijeve klijetke kod neoperiranih bolesnika. U postoperativnom praćenju nužno je prepoznati kasne restenoze, progresivne aortne regurgitacije te ostale komplikacije (kao što su aritmije ili smetnje provođenja). Da bi se vrijeme intervencija optimiziralo, u cijelom je procesu važna uloga heart tima u specijaliziranom centru za prirođene srčane bolesti u odraslih.

Discussion

Based on the patient's issues, the hemodynamic performance of the valve, and the existing pathology of coronary arteries, which was certainly at least one part of the cause of the symptoms, it was clear that another intervention was necessary. However, the decision was not easy. This is where the so-called "heart team", composed of the patient's cardiologist, echo sonographer, interventional cardiologist, and cardiovascular surgeon, offered ample assistance. The risk of the operation was high, the planned surgery quite extensive, and the outcome questionable because it was clear that even after myectomy it would be impossible to implant a much bigger valve, whereas the pronounced hypertrophy of myocardium, which can lead to diastolic dysfunction, could still cause difficulties and limit the patient in everyday activities. Additionally, there was the question of the "life expectancy" of the artificial ventricle and the likelihood of a third reoperation later in the patient's life. If the vicious cycle is not severed however, the pressure overload and ischemia will lead to progressive hypertrophy and fibrosis, and later to intractable heart failure. Although the clinical course after the second operation has so far been favorable, in the long-term we are faced with monitoring the valve function, the dimensions of the ascending aorta – which is at this time not dilated, controlling the arterial pressure, prophylaxis of endocarditis, and solving all other comorbidities we expect due to aging.

Conclusion

Extensive clinical experience on the incidence of the disease and generally favorable clinical outcome must not deceive us into "losing track" of a patient with a slow disease progression or who has already undergone intervention, because this is still a young and vulnerable population with a normal life expectancy and with it good quality of life. Therefore, it is important to keep in mind all the possible complications of the disease itself as well as the complications of the interventions performed, and provide continuous supervision. This primarily applies to echocardiographic monitoring of the progression of aortic stenosis and regurgitation, monitoring of the aortic dimension, and assessment of the size and function of the left ventricle in patients that have not yet been operated on. In postoperative monitoring it is important to recognize late restenosis, progressive aortic regurgitation, and other complications (such as arrhythmia or flow disturbances). In order to optimize intervention time, the role of the heart team in specialized centers for adult congenital heart diseases is important to the entire process.

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